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EXAMINER	
REIDEL, JESSICA L	

ART UNIT	PAPER NUMBER
3766	

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12/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/788,906	GIROUARD ET AL.	
	Examiner	Art Unit	
	JESSICA REIDEL	3766	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-38,41-148 and 150-152* is/are pending in the application.

4a) Of the above claim(s) *4-7,14-38 and 41-148* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10-13 and 150-152* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/11/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgment is made of Applicant's Amendment, which was received by the Office on September 11, 2008. Claims 8, 9, 39, 40 and 149 have been cancelled. Claim 152 is new and has been added. Claims 1-7, 10-38, 41-148 and 150-152 are currently pending.

Election/Restrictions

2. Claims 4-7, 14-38, 41-148 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement(s) in the replies filed on October 26, 2005 and May 21, 2008.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on September 11, 2008 has been acknowledged and considered by the Examiner. Applicant should note that the large number of references cited (both previously and newly submitted) have been considered by the Examiner in the same manner as other documents in Office search files are considered by the Examiner while conducting a search of the prior art in a proper field of search. See MPEP § 609.05(b). As previously requested in the Non-Final Rejection of April 26, 2007, in the Final Rejection of December 4, 2007, and in the Non-Final Rejection of June 11, 2008, Applicant is respectfully requested to indicate any references of those cited which they believe may be of particular relevance of the claimed invention.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the Applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the Applicant for patent or (2) a patent granted on an application for

patent by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. ***Claims 1, 2, 13 and 150-152 are rejected under 35 U.S.C. 102(a) and under 35 U.S.C. 102(e) as being anticipated by Padua et al. (U.S. 2003/0204206) (herein Padua).*** As to Claims 1, 2, 13 and 152, Padua expressly discloses a system 22 for controlling and regulating production and delivery of therapeutic genes/products comprising one or more sensors for sensing physiological signals indicative of a predetermined cardiac condition and a sensing element, read as an event detector 17, adapted to detect a predetermined cardiac condition (i.e. ischemia or reduced blood flow onset) from one or more of the sensed physiological signals and adapted to produce one or more conditions parameters related to the type of the predetermined condition. The conditions parameters (e.g., ST segment elevation or reduction of blood blow in the coronary sinus) are used in a closed-loop control algorithm of the system 22 (see Padua Figs. 11 and 12, page 11, paragraphs 162 and 164, page 12, paragraphs 170-171 and 173 and page 13, paragraphs 181-183). The system 22 of Padua further comprises a gene regulatory signal delivery device (output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12) that emits, in response to a gene regulatory control signal, an electric field as a "regulatory signal" which regulates transcription from a regulatable transcriptional control element (i.e. an electrically responsive promoter) in an expression vector (i.e. a plasmid, adenovirus vector, retrovirus vector or the like) having the regulatable transcriptional control element operably linked to an open reading frame, the expression of which treats the predetermined cardiac condition. Padua specifies that the system 22 provides for introducing into at least one cell of a patient, a vector containing an electrically responsive element (ERE) operably linked to a promoter to form an electrically responsive promoter (ERP) that modulates transcription of an operably linked therapeutic product in a cell upon delivery of the electric field regulatory signal to the ERP.

Specifically, the genetically engineered ERP is operably linked to a therapeutic gene sequence, the expression of which is controlled by the electric field regulatory signal emitted by the gene regulatory delivery device of the system 22 (see Padua page 1, paragraphs 1-9, page 2, paragraphs 11-12, pages 3-6, paragraphs 59-105, pages 8-10, paragraphs 117-144, page 11,

paragraphs 156-161 and page 13, paragraphs 177-180). A "controller" (micro-processor and memory circuitry 15 of Padua Fig. 11 or microcomputer unit 78 of Padua Fig. 12) may be coupled to the one or more sensors and is electrically connected to the gene regulatory signal delivery device (either output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12) for producing a gene regulatory control signal (such as trigger signal provided by digital controller/timer circuit 92). In particular, the controller of the system 22 is adapted to produce the gene regulatory control signal for quantitatively controlling and regulating the electric field regulatory signal. In one embodiment of the system 22 of Padua, the quantitative control is triggered automatically based on the controller of the system 22 receiving the one or more condition parameters related to a type of the predetermined cardiac condition from the event detector 17 (see Padua page 12, paragraph 173). Padua specifies that the system 22 provides "controlled delivery of therapeutic gene products" and that electric field regulatory signal emitted by the gene regulatory signal delivery device of the system 22 "is used to closely modulate the time, frequency, and delivery amount of a given therapeutic product". The emitted electric field regulatory signal is specifically used as a means to control the expression of ERPs that have been transplanted or incorporated into the tissue of a mammal and "controlled expression" is accomplished by closely regulating the emitted electric field regulatory signal through use of the system's controller (see Padua page 1, paragraph 5). In particular, the triggered regulatory control signal may include parameters that quantitatively control emission of the electric field regulatory signal where the parameters include predetermined timing and wave shape parameters for providing a "therapeutically effective amount" or "pharmacologically effective stimulus" for treating the predetermined cardiac condition (see Padua page 5, paragraphs 84 and 88-91, page 9, paragraphs 131-135, page 11, paragraphs 156-161, page 13, paragraphs 179-180 and page 14, paragraph 202).

6. As to Claim 150, in addition to the arguments previously presented, in some embodiments of Padua, the vector is not "part of an implantable device". Padua expressly discloses that the ERP constructs can be delivered directly to tissues of cells of the patient in vivo through the use of an appropriate gene delivery vector (viral or non-viral) through direct injection into the target tissue or through intravenous injection through a catheter (see Padua page 1, paragraph 5 and pages 9-10, paragraphs 131-144).

7. As to Claim 151, in addition to the arguments previously presented, the controller comprises a timer circuit (see Padua Fig. 12 and page 12, paragraph 168) adapted to time a predetermined time period of delivery time during which the gene regulatory signal delivery device emits the regulatory signal/signals (i.e. when a triggering event occurs, as previously discussed). Padua expressly discloses that the controller of the system 22 is used to closely modulate the time, frequency and delivery amount of the therapeutic product and the locus of delivery and specifies that delivery of the therapeutic product can be controlled by the location of the electrodes and the period of electrical stimulation (see Padua page 1, paragraph 5 and page 9, paragraph 136). The triggered regulatory signals are quantitatively regulated through predetermined timing and wave shape parameters defined by the controller and its timer circuit (see Padua page 12, paragraphs 172-173).

8. ***Claims 10-12 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as anticipated by Padua or, in the alternative, under 35 U.S.C. 103(a) as obvious over Padua in view of Donahue et al. (U.S. 2002/0155101) (herein Donahue).*** In addition to the arguments previously presented, Padua expressly discloses that implantable pulse generators that are well known in the art may be modified to stimulate the injected/implanted/introduced ERP-cells in accordance with the teachings of the implantable medical device system 22 of Figs. 11 and 12 including a wide variety of microprocessor based implantable pacemakers and implantable pacemaker/cardioverter/defibrillators (see Padua page 11, paragraph 166). A plurality of the implantable pacemakers and implantable pacemaker/cardioverter/defibrillators cited by Padua at page 11, paragraph 166 include event detection circuitry which comprise atrial and ventricular fibrillation detectors such as ***Bardy (U.S. 5,314,430).*** Furthermore, Donahue teaches that it is well known in the art to use a regulatable transcriptional control element in cardiac gene therapy for treatment of any of the following: sinus bradycardia, sinus tachycardia, atrial tachycardia, atrial fibrillation, atrial flutter, atrioventricular nodal block, atrioventricular node reentry tachycardia, atrioventricular reciprocating tachycardia, ventricular tachycardia or ventricular fibrillation (see Donahue page 7, paragraph 94). Donahue also discloses that practice of the invention is broadly compatible with one or a combination of different administration systems (see Donahue page 7, paragraph 88) for more effective and flexible anti-arrhythmic therapies by providing therapeutic methods for administering one or more therapeutic polynucleotides to the

heart under conditions sufficient to modulate (increase or decrease) at least one heart electrical property. Donahue further discloses that the invention modulates heart electrical conduction, reconfigures all or part of the cardiac action potential (AP) and reduces or avoids significant disruption of normal electrical function (see Donahue page 2, paragraph 14). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Padua in view of Donahue to administer the gene therapy upon detection of an atrial fibrillation or ventricular fibrillation to better the system's capabilities of eliminating a wide variety of predetermined cardiac conditions.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. ***Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Padua.*** Padua discloses the essential features of the claimed invention except that it is not specified that the gene regulatory signal delivery device emit an electromagnetic field regulatory signal. Instead, as previously discussed, the gene regulatory signal delivery device of the system 22 (either output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12) is coupled to unipolar or bipolar electrodes for forming an electric field generator that emits an electric field as the gene regulatory signal for controlling and regulating the ERP (see, for example, Padua page

2, paragraph 21, page 3, paragraph 60, page 10, paragraphs 145-150 and page 13, paragraph 179). At the time the invention was made, it would have been an obvious matter of design choice to a person of ordinary skill in the art to modify the gene regulatory signal delivery device of the system taught Padua such that it comprises an electromagnetic field generator for emitting an electromagnetic field as the gene regulatory signal, because Applicant has not disclosed that such modification provides an advantage, is used for a particular purpose or solves a stated problem. Furthermore, the Examiner considers electromagnetic field generators for emitting electromagnetic fields as gene regulatory signals to be conventional and well known in the art of gene therapy for regulating gene expression. The Examiner cites ***Goodman et al. (U.S. 2002/0099026)***, ***Kaplitt et al. (U.S. 2003/0087264)*** and ***Brighton (U.S. 2004/0073260)*** as being just three examples. Accordingly, one of ordinary skill in the art would have expected the system of Padua, and Applicant's invention, to perform to perform equally well with the emitted electric field gene regulatory signal as taught by Padua or the claimed electromagnetic field gene regulatory signal, because both signals would perform the same function of controlling and regulating gene expression in a patient via electrical devices equally well. Therefore, it would have been prima facie obvious to modify Padua to obtain the invention as specified in Claim 3 because such a modification would have been considered a mere design consideration which fails to patentably distinguish over the prior art of Padua.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. ***Claims 1-3, 10-13, 150 and 151 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-36, 38-74, 76-78 and 96-111 of copending Application No. 10/890,825 (Amended August 11, 2008) in view of Padua.*** Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof. As to Claim 1 of the current application, Application No. 10/890,825 also claims an implantable medical system, comprising a sensor to sense a physiological signal indicative of a predetermined cardiac condition, an event detector, coupled to the sensor, to detect the predetermined cardiac condition from the physiological signal, an implant telemetry module to receive an external command and an implant controller coupled to the event detector and the implant telemetry module, the implant controller including a gene or protein delivery control module adapted to produce an electrical signal to control gene or protein delivery in response to the predetermined cardiac condition and the external command. Similar analysis may be applied to the remaining dependent claims of the current application upon inspection of the conflicting and pending claims of copending Application No. 10/890,825.

The co-pending application includes synonymous limitations, as discussed, except does not specify that the protein delivery be provided by a regulatable transcriptional control element (i.e. an electrically responsive promoter (ERP)) in an expression vector (i.e. a plasmid, adenovirus vector, retrovirus vector or the like) having the regulatable transcriptional control element operably linked to an open reading frame, the expression of which produces the protein. Padua, however, teaches that the use of such ERP-cells is conventional and known in the art for providing selective and regulated gene therapy in a patient (see those sections of Padua cited above in this Office Action). Therefore, it would have been obvious to one having ordinary skill in the art, at the time the invention was made, to modify the claims of co-pending Application No. 10/890,825 such that the protein production is provided by an electrically responsive

promoter (ERP) in an expression vector having the ERP operably linked to an open reading frame, the expression of which produces the protein, as taught by Padua, since such a modification would provide selective and regulated gene therapy. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. ***Claims 1-3, 10-13, 150 and 151 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18, 32 and 33 of copending Application No. 11/220,397 (Amended October 21, 2008).*** Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof. As to Claim 1 of the current application, Application No. 11/120,397 also claims a sensing circuit to sense one or more parameters indicative of an ischemic event, an ischemia detector, coupled to the sensing circuit, to detect the ischemic event from the one or more parameters, a gene regulatory signal delivery device adapted to emit at least one gene regulatory signal that regulates transcription from a regulatable transcriptional control element within a vector and operably linked to an open reading frame and a controller coupled to the ischemia detector and the gene regulatory signal delivery device, the controller adapted to quantitatively control the emission of the regulatory signal from the gene regulatory signal delivery device. Similar analysis may be applied to the remaining dependent claims of the current application upon inspection of the conflicting and pending claims of copending Application No. 11/120,397. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. ***Claims 1-3, 10-13, 150 and 151 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-41 of copending Application No. 11/276,077.*** Although the conflicting claims are not identical, they are not patentably distinct from each other because the current claims are either a broadening of the scope of the patented claims or an obvious variant thereof. As to Claim 1 of the current application, Application No. 11/276,077 also claims a sensing circuit to sense one or more parameters indicative of an event, a gene regulatory signal delivery device adapted to emit at least one gene regulatory signal that regulates transcription from a regulatable transcriptional

control element within a vector and operably linked to an open reading frame and a controller coupled to the ischemia detector and the gene regulatory signal delivery device, the controller adapted to quantitatively control the emission of the regulatory signal from the gene regulatory signal delivery device. Similar analysis may be applied to the remaining dependent claims of the current application upon inspection of the conflicting and pending claims 1-41 of copending Application No. Application No. 11/276,077. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

16. Applicant's arguments filed September 11, 2008 have been fully considered but they are not found persuasive. Applicant argues that Padua does not "provide the claimed subject matter" and that Padua fails to disclose a controller adapted to (1) produce a gene regulatory control signal (2) transmit the gene regulatory signal to a gene regulatory signal delivery device to trigger an emission of a regulatory signal in response to a detection of a predetermined cardiac condition, and (3) quantitatively control the emission of the regulatory signal based on one or more condition parameters. Applicant further argues that "with 'predetermined parameters', the alleged controller of Padua does not quantitatively control emission of the regulatory signal based on one or more condition parameters" (see pages 22-23 of the Remarks). The Examiner respectfully disagrees. Padua expressly discloses a system 22 "to closely modulate the time, frequency, and delivery amount of a given therapeutic product and to closely define the locus of delivery", such that tissues containing genetically engineered cells that have received ERP elements direct the expression of a therapeutic gene or product upon receiving electrical stimulation (see, for example, Padua page 1, paragraphs 1-5 and paragraph 9). Applicant's attention is specifically directed to the second column of paragraph 5 where Padua states:

> The present invention describes a novel system to utilize an electrical stimulus (provided by an electrical pulse generator) as a means to control the expression of electrically responsive promoters (ERPs) that have been transplanted or incorporated into the tissue of a mammal. The target gene of interest is operably linked to an electrically responsive promoter sequence to provide controlled expression by the ability to closely regulate the electrical stimulus. The ERP gene constructs can be delivered by standard gene transfection methods to cells grown in culture and then implanted into the patient, or delivered directly to tissues or cells in vivo through the use of an appropriate gene delivery vector (viral or non-viral). Implantable electrodes operably coupled to the pulse generator can then be used to electrically stimulate at a defined locus the

> electrically responsive promoters in transfected or transplanted cells, which consequently results in the controlled expression of operably linked DNA sequences.

Upon review of paragraphs 1-5 and 9 of the Padua reference it is clear that the "controlled expression" is accomplished via the ability "to closely regulate the electrical stimulus" and that "the ability to regulate the expression of the gene of interest" allows for "controlling the dose and duration of the targeted therapeutic product". Although the parameters of the regulatory signal of Padua may be "predetermined", such predetermined parameters are used upon activation "on demand" upon detection of a predetermined cardiac condition *to subsequently provide quantitative control and regulation of the electric field regulatory signal for quantitatively controlling and regulating the delivery of therapeutic gene products* based upon the one or more condition parameters related to the type of predetermined cardiac condition for providing a "therapeutically effective amount" or "pharmacologically effective stimulus" to treat the predetermined cardiac condition (emphasis added).

17. Controller (micro-processor and memory circuitry 15 of Padua Fig. 11 or microcomputer unit 78 of Padua Fig. 12) of the system 22 taught by Padua may be coupled to the one or more sensors and electrically connected to the gene regulatory signal delivery device (either output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12). In particular, the controller of the system 22 is adapted to produce the gene regulatory control signal for quantitatively controlling and regulating the electric field regulatory signal emitted by the gene regulatory signal delivery device (either output circuit 12 or Padua Fig. 11 or output pulse generator 74 of Padua Fig. 12). In one embodiment of the system of Padua, the quantitative control is triggered automatically based on the controller of the system 22 receiving the one or more condition parameters from the event detector 17 of the system 22 (see Padua page 12, paragraph 173). Padua specifies that the system 22 provides "controlled delivery of therapeutic gene products" and that electric field regulatory signal emitted by the gene regulatory signal delivery device of the system 22 "is used to closely modulate the time, frequency, and delivery amount of a given therapeutic product" for a predetermined cardiac condition. The emitted electric field regulatory signal is specifically used as a means to control the expression of ERPs that have been transplanted or incorporated into the tissue of a mammal and "controlled expression" is accomplished by closely regulating the emitted electric field regulatory signal

through use of the system's controller (see Padua page 1, paragraph 5). In particular, the triggered regulatory control signal may include predetermined parameters that quantitatively control emission of the electric field regulatory signal where the parameters include predetermined timing and wave shape parameters for providing a "therapeutically effective amount" or "pharmacologically effective stimulus" for treating a type of predetermined cardiac condition based upon receipt of the one or more condition parameters related to the type of the predetermined cardiac condition (see Padua page 5, paragraphs 84 and 88-91, page 9, paragraphs 131-135, page 11, paragraphs 156-161, page 13, paragraphs 179-180 and page 14, paragraph 202). It is exceptionally unclear to the Examiner how the combined "temporal control" and "spatial control" discussed at page 9, paragraphs 131-135 and page 11, paragraphs 156-164 of the Padua reference is not synonymous with the quantitative control defined by the claims of the instant application, since the combined "temporal control" and "spatial control" of the Padua reference is specified as being provided by: (1) defining an electric field regulatory signal having predetermined timing and wave-shape parameters for providing the "therapeutically effective amount" or "pharmacologically effective stimulus" for treating a type predetermined cardiac condition; and (2) providing the defined electric field regulatory signal to the ERPs to transcribe the therapeutic gene(s) or product(s) for treating the predetermined cardiac condition *when* automatically triggered by the controller of the system 22 *upon* event detector 17 of the system 22 detecting the predetermined cardiac condition and providing the one or more condition parameters related to a type of the predetermined cardiac condition to the controller of the system 22 (emphasis added). In summary, the event detector 17 of Padua is configured to detect a predetermined cardiac condition and to produce one or more condition parameters related to *a type* of the predetermined cardiac condition and the recited controller of the system 22 disclosed by Padua is configured to produce the gene regulatory control signal, to transmit the gene regulatory control signal to the gene regulatory signal delivery device of the system 22 to trigger an emission of the electric field regulatory signal in response to a detection of the predetermined cardiac condition, and to quantitatively control the emission of the electric field regulatory signal based on the one or more condition parameters related to the *type* of the predetermined cardiac condition (emphasis added). In order to overcome the Padua reference, the Examiner suggests that Applicant modify Claim 1 such that the recited event detector is defined as being

"*configured* to detect the predetermined cardiac condition from the sensed physiological signal and to produce one or more condition parameters related to *a degree* of the predetermined cardiac condition" and such that the recited controller is defined as being "*configured* to produce the gene regulatory control signal, to transmit the gene regulatory control signal to the gene regulatory signal delivery device to trigger an emission of the regulatory signal in response to a detection of the predetermined cardiac condition, and to quantitatively control the emission of the regulatory signal based on the one or more condition parameters related to *the degree* of the predetermined cardiac condition" (emphasis added).

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. ***Shafer (U.S. 2005/0123526)*** teaches that expression of a target gene, which may encode a gene product that promotes proliferation, differentiation, migration, or integration of an exogenous stem cell transplanted into the central nervous system (CNS), may be closely controlled by application of a controlled and defined electrical signal of the appropriate type and energy. ***Mika et al. (U.S. 2007/0027487)*** expressly disclose an apparatus (120) for modifying gene expression in cardiac muscle cells (110), by the application of electric fields, and further specify that it is important that the apparatus be adapted to take an effect of the gene expression into account in its functioning such that electrically induced gene expression may be modified by modulation of the applied electric fields and/or halted by halting ceasing application of the electric fields.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JESSICA REIDEL whose telephone number is (571)272-2129. The Examiner can normally be reached on Monday - Friday, 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Carl H. Layno can be reached on (571)272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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